WEST Search History

Hide Items Restore Clear Cancel

DATE: Friday, March 19, 2004

Hide?	<u>Set</u> Name	Query	<u>Hit</u> Count
	DB=P	GPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=OR	
	L6	L5 and (vaccine or adjuvant or immuno\$)	67
	L5	12 not 14	141
	L4	L3 and 12	23
	L3	L1 and (QS-21 or QS21 or QA-21 or QA21)	351
	L2	L1 and (weight with ratio)	164
	L1	(\$6sterol) same (saponin or QS-21 or QS21 or QA-21 or QA21 or Quil adj A or (Quil adj A or sapon\$5) same (QS\$3 or QA\$3))	951

END OF SEARCH HISTORY

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FILE 'HOME' ENTERED AT 13:52:54 ON 19 MAR 2004
     QUE (######STEROL) AND (QUIL (A) A OR SAPONIN OR SAPONARIA OR QS-21 OR QS2
L1
         1 OR QA-21 OR QA21)
            59 L2 AND (QS21 OR QS-21 OR QA-21 OR QA21 OR (QS OR QA) (A) 21)
L4
          1315 L3 AND (CHOLESTEROL) (S) (QUIL (A) A OR SAPONIN OR SAPONARIA
L8
               OR QS-21 OR QS21 OR QA-21 OR QA21)
     (FILE 'HOME' ENTERED AT 13:52:54 ON 19 MAR 2004)
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     BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS,
     DDFB, DDFU, DGENE, DRUGB, DRUGMONOG2, ... 'ENTERED AT 13:53:10 ON 19 MAR
     2004
                QUE (######STEROL) AND (QUIL (A) A OR SAPONIN OR SAPONARIA OR Q
L1
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     13:57:48 ON 19 MAR 2004
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L2
           2209 S L2 AND CHOLESTEROL
L3
             59 S L2 AND (QS21 OR QS-21 OR QA-21 OR QA21 OR (QS OR QA) (A) 21)
L4
L5
             57 S L3 AND L4
             41 DUP REM L5 (16 DUPLICATES REMOVED)
L6
1.7
              2 S L6 AND PY<1998
           1315 S L3 AND (CHOLESTEROL) (S) (QUIL (A) A OR SAPONIN OR SAPONARIA
L8
             21 S L3 AND (WEIGHT (S) RATIO)
L9
             14 DUP REM L9 (7 DUPLICATES REMOVED)
L10
            321 S L1 AND (IMMUNO########## OR ADJUVANT OR VACCINE)
L11
            294 S L11 AND L3
L12
L13
             59 S L11 AND L4
L14
            57 S L12 AND L13
L15
            41 DUP REM L14 (16 DUPLICATES REMOVED)
              0 S L15 NOT L6
L16
L17
            997 S L8 AND PY<1998
            549 DUP REM L17 (448 DUPLICATES REMOVED)
L18
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L19

L20

L21

37 S L18 AND L11

36 S L19 NOT L15 2 S L18 AND L9 AN 97088741 MEDLINE PubMed ID: 8934649 DN ISCOMs (immunostimulating complexes): the first decade. Barr I G; Mitchell G F AU CSL Limited, Parkville, Victoria, Australia. CS Immunology and cell biology, (1996 Feb) 74 (1) 8-25. Ref: 152 SO Journal code: 8706300. ISSN: 0818-9641. CY Australia Journal; Article; (JOURNAL ARTICLE) DT General Review; (REVIEW) (REVIEW, ACADEMIC) LΑ English FS Priority Journals EM199701 Entered STN: 19970219 Last Updated on STN: 19970219 Entered Medline: 19970124 A little over a decade ago, novel immunostimulating complexes AΒ (ISCOMs) were described. This review examines the position and progress that ISCOM technology has achieved in the fields of vaccine research and medicine over this period. Much of the work on ISCOMs has remained in the area of vaccine research where there is still an urgent need for improved adjuvants to help combat important diseases such as AIDS, malaria and influenza. Currently the only widely licensed adjuvants for human use are the aluminium salts, but with the trend towards highly purified subunit vaccines, which are inherently less immunogenic than some of the older vaccines, potent adjuvants capable of promoting specific immune responses are required. ISCOMs are one such technology that offers many of these requirements and as their use in vaccines enters its second decade clinical trials are commencing that will establish whether these submicron, non-living particles composed of saponin , cholesterol, phospholipid and in many cases protein, are useful components for a range of human vaccines. ANSWER 9 OF 36 MEDLINE on STN L20 90237592 MEDLINE ΑN DN PubMed ID: 2634709 Quaternary structure of the immunostimulating complex (iscom). TIOzel M; Hoglund S; Gelderblom H R; Morein B ΑU Robert Koch-Institute of the Federal Health Office, Berlin, Federal CS Republic of Germany. Journal of ultrastructure and molecular structure research, (1989 SO Dec) 102 (3) 240-8. Journal code: 8612238. ISSN: 0889-1605. CY United States DTJournal; Article; (JOURNAL ARTICLE) LΑ English Priority Journals; AIDS FS EM199006 Entered STN: 19900706 ED Last Updated on STN: 19970203 Entered Medline: 19900607 Proteins of either HIV-1, hepatitis B, or rabies virus were incorporated AΒ with the adjuvant substance Quil A and cholesterol into the immunostimulating complex: iscom. Formation and symmetry of this regular complex were analyzed by electron microscopy. Micellar structures with a diameter of about 12 nm,

MEDLINE on STN

L20

ANSWER 3 OF 36

occasionally with a 7-nm stain-filled center, were formed in a 0.03% water suspension of Quil A. Cavities or holes appeared in the smooth structures of cholesterol upon the addition of Ouil A, and after mixing Quil A and cholesterol 1:1 fragile and flattened structures of matrix were produced with a diameter of about 40 nm. By freeze-drying the matrix was preserved as a cage-like, isometric particle. Stable iscom particles composed of Quil A, cholesterol, and selected viral proteins had an approximate diameter of 32 nm. particles had an uniform, cage-like structure, exhibiting icosahedral symmetry, irrespective of the viral proteins incorporated. Tilting experiments and rotational image analysis indicated that the iscoms were composed of 20 morphological subunits assembled in a pentagonal dodecahedron with a hole on each of the 12 pentagonal faces. symmetrical shape of the iscom might explain both its remarkable stability and its capacity to efficiently present antigens to the immune system.

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MEDLINE on STN
    ANSWER 10 OF 36
L20
```

MEDLINE AN88251637

DN PubMed ID: 2838046

- The requirement of lipids for the formation of immunostimulating TΤ complexes (iscoms).
- Lovgren K; Morein B ΑU
- National Veterinary Institute, Department of Virology, Biomedicum, CS Uppsala, Sweden.
- Biotechnology and applied biochemistry, (1988 Apr) 10 (2) SO 161-72.

Journal code: 8609465. ISSN: 0885-4513.

- CYUnited States
- Journal; Article; (JOURNAL ARTICLE) DT
- LΑ English
- FS Priority Journals
- 198808 EM

AR

EDEntered STN: 19900308

> Last Updated on STN: 19900308 Entered Medline: 19880803

The iscom--immunostimulating complex--is a highly immunogenic formulation of microbial membrane antigens. The biochemically analyzed components of the iscom are the protein and the glycoside Quil A. Continued analysis of the iscom showed that the protein moiety--the antigen--does not contribute to the iscom as a construct. Instead, cholesterol and Quil A are the essential structural components assembled together into a typical cage-like structure. A more "fluid" lipid, such as phosphatidylcholine, is needed to facilitate the incorporation of amphipathic poly- or oligopeptides into the iscom matrix.

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L20
    ANSWER 15 OF 36
                         MEDLINE on STN
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- 81025618 MEDLINE AN
- PubMed ID: 7419284 DN
- Saponin and other haemolysins (vitamin A, aliphatic amines, ΤI polyene antibiotics) as adjuvants for SRBC in the mouse. Evidence for a role for cholesterol-binding in saponin adjuvanticity.
- ΑU Bomford R
- International archives of allergy and applied immunology, (1980) SO 63 (2) 170-7.
 - Journal code: 0404561. ISSN: 0020-5915.
- CYSwitzerland
- DTJournal; Article; (JOURNAL ARTICLE)

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ΤA
     English
FS
     Priority Journals
EM
     198012
     Entered STN: 19900316
ED
     Last Updated on STN: 19900316
     Entered Medline: 19801216
     The hypothesis that the adjuvant, as well as the haemolytic,
AB
     activity of saponin depends on binding to cholesterol
     in cell membranes is supported by showing that cholesterol
     absorbs out adjuvant activity, and inhibits
     immunopotentiation in vivo when added to the injection mixture.
     Also, out of a range of haemolytic substances, chosen for their known
     properties as adjuvants or for cholesterol binding,
     the only materials which displayed a comparable activity to
     saponin were the polyene antibiotics Nystatin and Amphotericin B,
     whose binding to membrane cholesterol causes similar
     morphological changes to that of saponin.
    ANSWER 16 OF 36 CAPLUS COPYRIGHT 2004 ACS on STN
L20
ΑN
     1996:410535 CAPLUS
DN
     125:56216
     Saponin preparations and use thereof in ISCOMs
TI
     Cox, John Cooper; Coulter, Alan Robert; Morein, Bror; Lovgren-Bengtsson,
IN
     Karin; Sundquist, Bo
PΑ
     Iscotec Ab, Swed.
SO
     PCT Int. Appl., 39 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
                                        APPLICATION NO. DATE
     PATENT NO.
                 KIND DATE
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     EP 785802
                     A1
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                           19941012
                      \mathbf{A}
     NZ 1995-293882
                      Α1
                           19951012
     WO 1995-AU670
                      W
                           19951012
     A preparation of saponins of Quillaja saponaria, comprises
AB
     fractions of Quil A having good adjuvant
     activity, low hemolytic activity and good ability to form
     immunostimulatory complexes (ISCOMs). Quil A
     fractions (QH-A.apprx.C and QH703) were purified from Quillaja bark extract,
     formed ISCOMs with cholesterol and/or phosphatidylcholine, and
     used as vaccine adjuvant for influenza virus HA or
     diphtheria toxoid. Interleukin 1 induction by various mixts. of Quillaja
     saponins induces, and clin. safety of ISCOM matrix prepared from
     QH703 in human were also demonstrated.
```

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L20 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2004 ACS on STN
     1991:542224 CAPLUS
AN
DN
     115:142224
TI
     Complexes having adjuvant activity in vaccine
     preparation
     Mackenzie, Neill Moray; O'Sullivan, Angela Marie
IN
     Cooper's Animal Health Ltd., UK
PA
SO
     Eur. Pat. Appl., 13 pp.
     CODEN: EPXXDW
DT
     Patent
     English
LΑ
FAN.CNT 1
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                      A1 19970409
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     EP 766967
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
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                                          US 1990-611543
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                      В
                                          LV 1993-753
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PRAI GB 1989-19819
                           19890901
    US 1989-426050
                           19891024
     EP 1990-309570
                           19900831
    WO 1990-GB1351
                           19900831
     "Empty" iscom (immuno-stimulating complexes) matrixes, ie.
     formed without an antigen, have been found to provide an adjuvant
```

AB "Empty" iscom (immuno-stimulating complexes) matrixes, ie.
formed without an antigen, have been found to provide an adjuvant
formation for a sep. antigen in a vaccine formulation, the
antigen being associated with a bacterium or mycoplasma. These and
conventional iscoms can be formed without removing the solubilizing agent
used for the antigen. In each case, the iscom can be 3-dimensional or, if
formed without phospholipid, 2-dimensional. The glycoside is preferably
Quil A and the sterol is preferably
cholesterol.

```
L20 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2004 ACS on STN
```

AN 1990:589646 CAPLUS

DN 113:189646

TI Adjuvant-lipid complexes for use as modified adjuvants in preparing vaccines

IN Buroru, Morein

PA Loevgren, Karin, Swed.

SO Jpn. Kokai Tokkyo Koho, 10 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

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KIND DATE
   PATENT NO.
                                       APPLICATION NO. DATE
    _____
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    JP 02092996
                   A2 19900403
                                        JP 1988-247295 19880930 <--
PΙ
                         19880930
PRAI JP 1988-247295
    The title complex adjuvant free of antigenic determinant
    activity is prepared by mixing cholesterol in organic solvents or
    detergent solns. with ≥1 hydrophobic saponins,
    adjuvants, and other lipids, and the mixture is dialyzed, gel
    filtrated, or electrophoresed to remove the organic solvents or detergent
    solns. The saponins are triterpenoid saponins, especially
    Quil A or its subfractions. Vaccines prepared
    with the modified adjuvant have min. side effects. Preparation of
    MDP (muramyl dipeptide) adjuvant peptide-
    phosphatidylethanolamine-cholesterol-phosphatidylcholine-
    Quil A complex is given as an example.
L20 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2004 ACS on STN
NΑ
    1987:605167 CAPLUS
\mathsf{D}\mathsf{N}
    107:205167
    Process for preparing immunological complexes and pharmaceutical
\Gamma I
    composition containing these complexes
ΙN
    De Vries, Petra; Van Wezel, Antonius Ludovicus; Beuvery, Eduard Coen
PΑ
    De Staat der Nederlanden Vertegenwoordigd Door de Minister van Welzijn,
    Volksgezondheid en Cultuur, Neth.
SO
    Eur. Pat. Appl., 13 pp.
    CODEN: EPXXDW
DΤ
    Patent
LΑ
    English
FAN.CNT 1
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                                       APPLICATION NO. DATE
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    EP 231039 A1 19870805
EP 231039 B1 19920108
PΙ
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    JP 63002933 A2
JP 2502558 B2
                         19880107
                                        JP 1987-7384
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    US 4900549
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PRAI NL 1986-66
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    EP 1987-200035
                          19870113
    An immunogenic complex is prepared by contacting an amphoteric
    antigenic protein or peptide in dissolved or solubilized form with a solution
    containing a detergent, a sterol, and a glycoside comprising
    hydrophobic and hydrophobic regions in at least the critical micelle forming
    concentration with subsequent removal of the detergent and purification of the formed
    immunogenic complex. Measles virus fusion protein was produced
    and purified by known methods and incorporated into an immunogenic
    complex by treating fusion protein (60 µg) with 180 µL Tris-HCl (pH
    7.8), 150 mM NaCl, 2% octylglucoside, and 350 \mug
    phosphatidylethanolamine and 350 \mu g cholesterol in 700 \mu L
    2% octylglucoside for 1 h at room temperature, addition of 1.7 mg Quil
    A (10% weight/volume), removal of octylglucoside by dialysis against 10
    mM Tris-HCl (pH 7.8) and 150 mM NaCl for 16 h at 4°, and purification
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FAN.CNT 1

via ultracentrifugation (continuous sucrose gradient), and electron microscope examination of the product-containing fractions (micrograph shown). L20 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2004 ACS on STN 1966:62261 CAPLUS 64:62261 OREF 64:11692c-d Research on saponin, an adjuvant substance and stimulant of immunity Richou, R.; Lallouette, P.; Jensen, R.; Belin, Cl. Revue d'Immunologie (1965), 29(4-5), 205-19 CODEN: RIMMAZ; ISSN: 0035-2454 Journal French Different lots of saponin (I) had different capacities in regard to hemolytic activity, lethal dose in mice, and inflammatory effect, with no relation between the 3 properties. I heated 0.5 or 1 hr. at 70° or 0.5 hr. at 100° was not changed in inflammatory capacity and lethal or hemolytic properties and no modification was seen in the capacity to stimulate immunity to staphylococci when used as an adjuvant. I neutralized by cholesterol lost most of its lethal action but was as active in provoking inflammation as I alone. Certain actions of I were compared to synthetic detergents and some common properties were found. L20 ANSWER 30 OF 36 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 1992:477030 BIOSIS PREV199294108405; BA94:108405 PREPARATION OF IMMUNOSTIMULATING COMPLEXES ISCOM CONTAINING BOVINE HERPESVIRUS 1 PROTEINS. FRANZ J [Reprint author]; HAMPL J; STEPANEK J; SMID B VET RES INST, 621 32 BRNO Acta Veterinaria Brno, (1992) Vol. 61, No. 1, pp. 37-41. CODEN: ACVTB9. ISSN: 0001-7213. Article BA ENGLISH Entered STN: 27 Oct 1992 Last Updated on STN: 27 Oct 1992 A method for obtaining ISCOMs with incorporated bovine herpesvirus 1 (BHV-1) proteins from various amounts of cholesterol, phosphatidylcholine and **Quil A** is described. highest virus protein incorporation rate obtained was 25%. Morphology of ISCOMs depended on amounts of Quil A, cholesterol and phosphatidylcholine used. A high immunogenicity of BHV-1-ISCOM, as compared with free virus-proteins, was confirmed experimentally in mice. L20 ANSWER 32 OF 36 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN 95159377 EMBASE 1995159377 Immunostimulating complexes. Clinical potential in vaccine development. Morein B.; Lovgren K.; Ronnberg B.; Sjolander A.; Villacres-Eriksson M. Swedish Univ. of Agricultural Scis., Faculty of Veterinary Medicine, Biomedical Centre, Box 585, S-751 23 Uppsala, Sweden Clinical Immunotherapeutics, (1995) 3/6 (461-475).

ΑN

DN

TI

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LΑ

AB

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DN

TI

ΑU CS

SO

DT

FS

LΆ

ED

AΒ

ANDN

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ΑU

CS

SO

ISSN: 1172-7039 CODEN: CIMMEA

New Zealand CYJournal; General Review DTMicrobiology FS 004 Immunology, Serology and Transplantation 026 Pharmacology 030 Drug Literature Index 037 English LΑ English SL An immunostimulating complex (iscom) is a particle containing AΒ several copies of an antigen, with a built-in adjuvant. It is constructed to provide a physically optimal presentation of antigen to the immune system. An iscom particle without incorporated antigen is called the iscom matrix, or just matrix, and can be used as a conventional adjuvant that is added to the antigen whose immunogenicity is to be reinforced. The unique components of the iscom matrix are saponins (triterpenoids) from the tree Quillaja saponaria , which exhibit a unique affinity for cholesterol and thereby facilitate the stability of the complex. The triterpenoids can be used as a crude preparation of Quillaja saponins or as purified preparations of Quillaja triterpenoids. The various triterpenoids have different characteristics, of which some are relevant to vaccine development such as the iscom-forming capacity, the immunomodulatory capacity, a low cell lytic property and low toxicity in general. Consequently, various compositions of triterpenoids, including efficient nontoxic adjuvant formulations or inert carrier formulations, can be made. The currently used iscom vaccine and experimental vaccines induce a broad immune response, including major histocompatibility complex (MHC) class I and II T cell responses. The MHC class II response encompasses a prominent response of T helper 1 (T(H)1)-like cells, producing interleukin (IL)-2 and interferon-y and favouring cell-mediated immunity. A T(H)2-like response may also be evoked, with cells producing IL-4 and IL-10 and promoting humoral immunity. However, the same influenza virus envelope antigen in a micellar nonadjuvanted torm induces a more prominent T(H)2 type of response, with cells producing more IL-10. The iscom particle is also an interesting nonreplicating candidate for induction of mucosal immunity. Iscoms containing different kinds of antigens in various experimental vaccines evoke secretory IgA or cytotoxic T cell responses when administered orally and intranasally. Experimental iscom vaccine formulations have been shown to induce protective immunity

- L20 ANSWER 35 OF 36 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
- AN 80:420831 SCISEARCH
- GA The Genuine Article (R) Number: KJ163
- TI SAPONIN AND OTHER HEMOLYSINS (VITAMIN-A, ALIPHATIC-AMINES, POLYENE ANTIBIOTICS) AS ADJUVANTS FOR SRBC IN THE MOUSE EVIDENCE FOR A ROLE FOR CHOLESTEROL-BINDING IN SAPONIN ADJUVANTICITY
- AU BOMFORD R (Reprint)
- CS WELLCOME RES LABS, DEPT EXPTL IMMUNOBIOL, BECKENHAM BR3 3BS, KENT, ENGLAND (Reprint)

to a number of micro-organisms, including viruses and retroviruses, parasites and bacteria, in several species, including primates.

- CYA ENGLAND
- SO INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1980) Vol. 63, No. 2, pp. 170-177.
- DT Article; Journal
- FS LIFE
- LA ENGLISH
- REC Reference Count: 25

L20 ANSWER 36 OF 36 TOXCENTER COPYRIGHT 2004 ACS on STN 1990:163339 TOXCENTER ANCopyright 2004 ACS CP DN CA11321189646F Adjuvant-lipid complexes for use as modified adjuvants ΤI in preparing vaccines Buroru, Morein ΑU ASSIGNEE: Loevgren, Karin CS JP 9092996 A2 3 Apr 1990 PI(1990) Jpn. Kokai Tokkyo Koho, 10 pp. SO CODEN: JKXXAF. CYSWEDEN DTPatent FS CAPLUS OS CAPLUS 1990:589646 LΑ Japanese Entered STN: 20040200 ED Last Updated on STN: 20040200 The title complex adjuvant free of antigenic determinant AΒ activity is prepared by mixing cholesterol in organic solvents or detergent solns. with ≥1 hydrophobic saponins, adjuvants, and other lipids, and the mixture is dialyzed, gel filtrated, or electrophoresed to remove the organic solvents or detergent solns. The saponins are triterpenoid saponins, especially Quil A or its subfractions. Vaccines prepared with the modified adjuvant have min. side effects. Preparation of

MDP (muramyl dipeptide) adjuvant peptide-

Quil A complex is given as an example.

phosphatidylethanolamine-cholesterol-phosphatidylcholine-

+







Search PubMed Nucleotide Protein Genome Structure OM

Search PubMed for #16 not #2

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Journals Br

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LinkOut
Cubby

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TOXNET
Consumer Health
Clinical Alerts
Clinical Trials gov
PubMed Central

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•	Search History	will be lo	st after e	eight hours	of inactivity.
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- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.

Search	Most Recent Queries	Time	Result
#17	Search #16 not #2	14:59:38	<u>22</u>
#16	Search #15 AND #13	14:58:04	22
#15	Search (sapon* or Quil A or QS-21 or qs21 or qa21 or qa-21) AND (stabil* or hydrol* or reactogen* or toxic*) Field: Title/Abstract	14:57:22	<u>688</u>
#14	Search (sapon* or Quil A or QS-21 or qs21 or qa21 or qa-21) AND (stabil* or hydrol* or reactogen* or toxic*)	14:53:36	<u>1585</u>
#13	Search #11 not #2 Field: Title/Abstract, Limits: Publication Date to 1997	14:52:33	<u>246</u>
#12	Search #11 not #2 Field: Title/Abstract, Limits: Publication Date to 1997	14:51:43	<u>246</u>
#11	Search cholesterol AND (sapon* or Quil A or QS-21 or qs21 or qa21 or qa-21) Field: Title/Abstract, Limits: Publication Date to 1997	14:51:12	<u>258</u>
#10	Search cholesterol AND (sapon* or Quil A or QS-21 or qs21 or qa-21) Field: Title/Abstract, Limits: Publication Date to 1998	14:50:23	273
#2	Search #1 AND (iscom or adjuvant or liposome) Field: Title/Abstract	14:49:51	<u>22</u>
#1	Search cholesterol AND (sapon* or Quil A or QS-21 or qs21 or qa21 or qa-21) Field: Title/Abstract	14:38:49	333

Clear History

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